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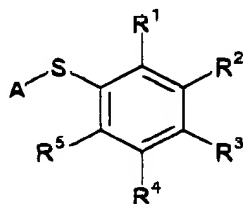
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IN THE SPECIFICATION:

Please enter the specification amendments as follows.

Beginning on page 4, line 8, and ending on page 6, line 14:

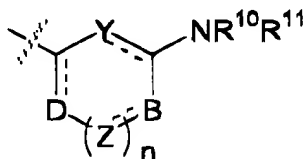
The present invention is directed to compounds of Formula I



Formula I

or pharmaceutically acceptable salts, optical isomers, or prodrugs thereof,

wherein R^1 , R^2 , R^3 , R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde, or a group of Formula II defined as



Formula II

subject to the proviso that one or more than one of R^1 or R^3 is a group of Formula II as defined above;

wherein D, B, Y and Z at each occurrence are independently selected from the group consisting of $-CR^6=$, $-CR^7R^8-$, $C(O)-$, $-O-$, $-SO_2-$, $-S-$, $-N=$, and $-NR^9-$;

n is an integer of zero to three;

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R⁶, R⁷, R⁸, and R⁹, at each occurrence, are each independently selected from the group consisting of hydrogen, alkyl, carboxy, hydroxyalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl and carboxyalkyl; and

R¹⁰ and R¹¹ are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, alkoxyalkyl, alkoxycarbonylalkyl, carboxyalkyl, hydroxyalkyl, heterocyclyl, heterocyclylalkyl and heterocyclylamino; or

R¹⁰ and R¹¹ are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring, substituted with one or more than one substituent R¹³, wherein R¹³, at each occurrence is independently selected from the group consisting of alkyl, alkylene, alkoxy, alkoxyalkyl, cycloalkyl, aryl, heterocyclyl, heterocyclylalkyl, heterocyclylcarbonyl, heterocyclylalkylaminocarbonyl, hydroxy, hydroxyalkyl, hydroxyalkoxyalkyl, carboxy, carboxyalkyl, carboxycarbonyl, carboxaldehyde, alkoxycarbonyl, arylalkoxycarbonyl, aminoalkyl, aminoalkanoyl, aminocarbonyl, carboxamido, alkoxycarbonylalkyl, carboxamidoalkyl, cyano, tetrazolyl, alkanoyl, hydroxyalkanoyl, alkanoyloxy, alkanoylamino, alkanoyloxyalkyl, alkanoylaminoalkyl, sulfonate, alkylsulfonyl, alkylsulfonylaminocarbonyl, arylsulfonylaminocarbonyl and heterocyclylsulfonylaminocarbonyl;

wherein A is an unsubstituted aryl group, an unsubstituted heterocyclyl group, a substituted aryl group, or a substituted heterocyclyl group, substituted with one or more than one substituent R¹², wherein R¹², at each occurrence, is independently selected from the group consisting of halogen, alkyl, aryl, haloalkyl, hydroxy, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxyalkoxy, hydroxyalkyl, aminoalkyl, aminocarbonyl, alkyl(alkoxycarbonylalkyl) aminoalkyl, heterocyclyl, heterocyclylalkyl, carboxaldehyde, carboxaldehyde hydrazone, carboxamide, alkoxycarbonylalkyl, carboxy, carboxyalkyl,

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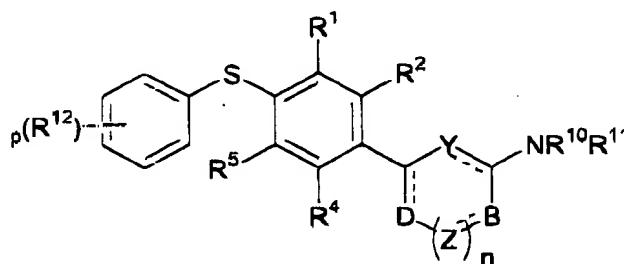
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carboxyalkoxy, carboxythioalkoxy, carboxycycloalkoxy, thioalkoxy, carboxyalkylamino, trans-cinnamyl, hydroxyalkylaminocarbonyl, cyano, amino, heterocyclylalkylamino, and heterocyclylalkylaminocarbonyl; and

wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 , R^{10} , R^{11} , R^{12} and R^{13} are unsubstituted or substituted with at least one electron donating or electron withdrawing group

Beginning on page 6, line 18 and ending on page 8, line 16:

The present invention is also directed to compounds of Formula III



Formula III

wherein R^1 , R^2 , R^3 , R^4 and R^5 are each independently selected from the group consisting of hydrogen, halogen, alkyl, haloalkyl, alkoxy, cyano, nitro, cycloalkyl and carboxaldehyde;

D, B, Y and Z are as defined above for Formula I;

R^{12} , at each occurrence, is independently selected from the group consisting of halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

p is an integer of zero to five; and

wherein R^1 , R^2 , R^4 , R^5 , R^{10} , R^{11} and R^{12} are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

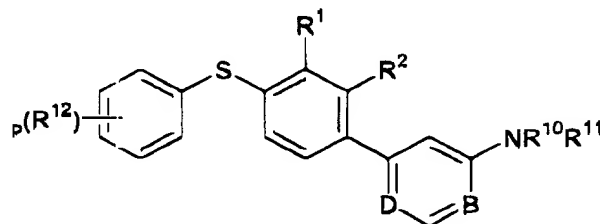
Presently most preferred, but not required, compounds of Formula III have p as one; R^4 and R^5 as hydrogen; R^{12} as halogen, alkyl, carboxyalkoxy, carboxyalkyl or heterocyclyl

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and R^{10} and R^{11} are taken together with N to form a three to seven membered unsubstituted heterocyclyl ring, or a three to seven membered substituted heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

Presently most preferred, but not required, compounds are of Formula IV



Formula IV

wherein D and B are each independently selected from the group consisting of $-N=$ and $-CR^6=$;

R^1 and R^2 are each independently selected from the group consisting of hydrogen, halogen and haloalkyl;

R^{10} and R^{11} are as defined above for Formula I;

R^{12} , at each occurrence, is independently selected from the group consisting of halogen, alkyl, haloalkyl, alkoxy, carboxyalkoxy, carboxyalkyl and heterocyclyl;

p is an integer of zero to five; and

wherein R^1 , R^2 , R^{10} , R^{11} , and R^{12} are unsubstituted or substituted with at least one electron donating group or electron withdrawing group.

Presently most preferred, but not required, compounds are of Formula IV, where p can be one; R^{12} can be halogen, alkyl, alkoxy, carboxyalkoxy, carboxyalkyl or heterocyclyl; and R^{10} and R^{11} can be taken together with N to form a three to seven membered heterocyclyl ring; said ring being piperidine, piperazine, morpholine, pyrrolidine or azetidine.

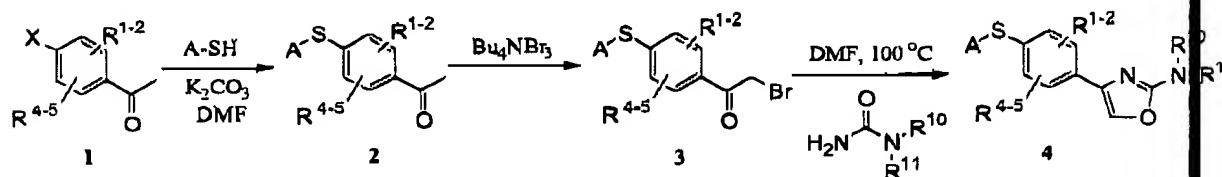
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Beginning on page 28, line 10, and ending on page 31, line 10:

Scheme 1 describes compounds of Formula I, which contain an oxazole ring ($n=0$, $Y=N$, $B=O$, $D=C$). In Scheme 1, and likewise in Schemes 2 and 4, the substituent X is a leaving group. In Scheme 1, Aryl methyl ketone 1, with an appropriate substitution (R^{1-2} and R^{4-5}), and a leaving group X , reacts with an aryl thiol to give a biaryl sulfide 2. Biarylsulfide 2 can be converted into an alpha-bromomethyl ketone 3 using a variety of reagents including Bu_4NBr_3 . Condensation of 3 with a urea gives a desired oxazole compound 4.

Scheme 1

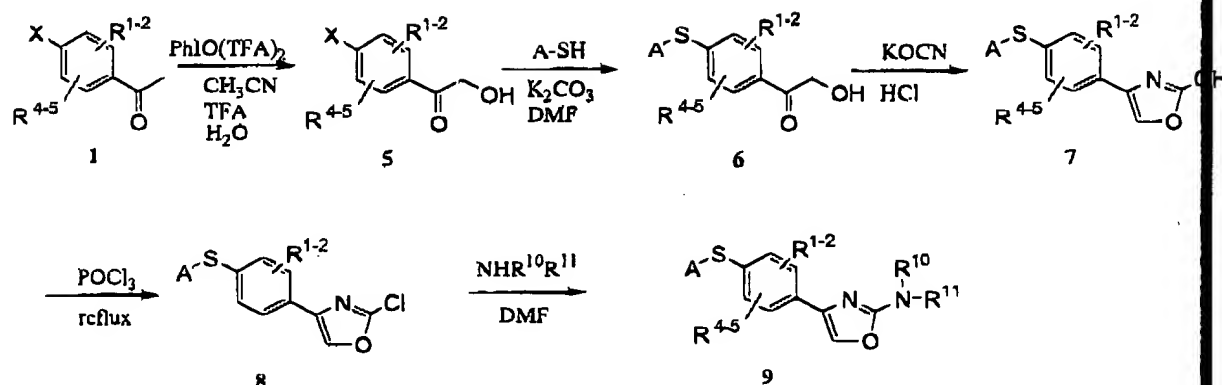


Another method of preparing compounds of Formula I containing an oxazole ring ($n=0$, $Y=N$, $B=O$, $D=C$) is illustrated in Scheme 2. In Scheme 2, an aryl methyl ketone 1 is converted into an alpha-hydroxymethyl ketone 5, which then can be reacted with an aryl thiol to give a biaryl sulfide 6. Acid-catalyzed condensation of 6 with $KOCN$ affords a 2-hydroxy oxazole 7, which can be converted into a 2-chloro-oxazole 8 using $POCl_3$. Displacement of the chloride of 8 with an amine gives a desired 2-amino-oxazole 9.

Scheme 2

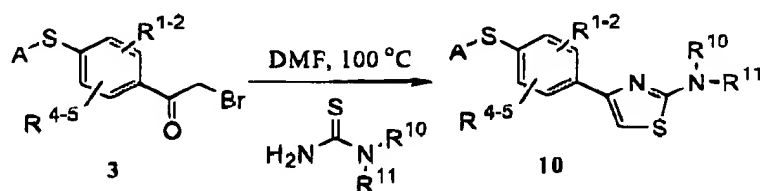
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Scheme 3 describes the synthesis of a class of compounds of Formula I containing a thiazole ring ($n=0$, $\text{Y}=\text{N}$, $\text{B}=\text{S}$, $\text{D}=\text{C}$). In Scheme 3, biaryl sulfide alpha-bromomethyl ketone 3 can be prepared following the procedure outline in Scheme 1. Condensation of 3 with a properly substituted thiourea gives a desired 2-aminothiazole 10.

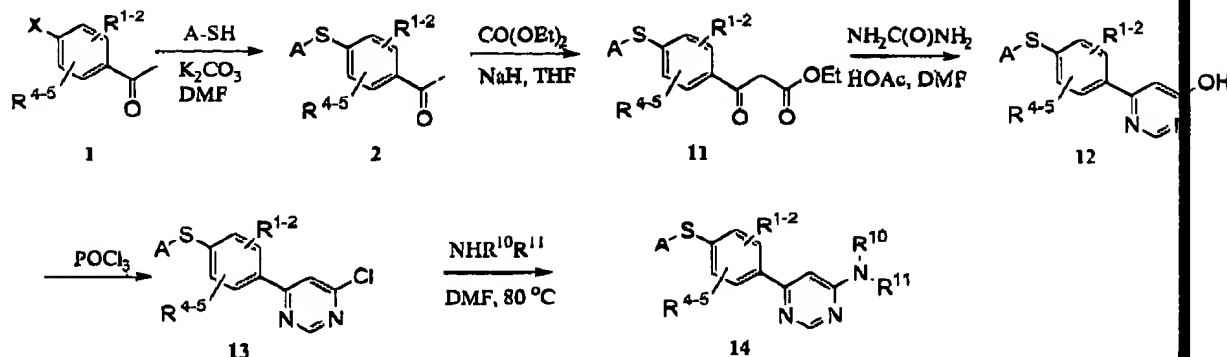
Scheme 3



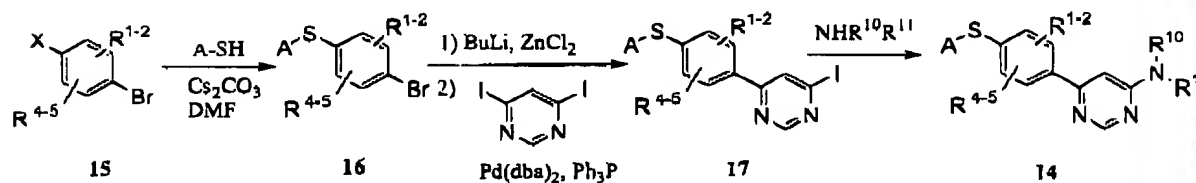
Another class of compounds of Formula I are compounds containing a pyrimidine ring, for example 4,6-disubstituted pyrimidines ($n=1$, $\text{Y}=\text{C}$, $\text{B}=\text{N}$, $\text{Z}=\text{C}$, $\text{D}=\text{N}$). Scheme 4 describes one procedure for the preparation of this class of compounds. Reaction of a biaryl sulfide methyl ketone 2 with diethyl carbonate under base-catalysis leads to a beta-ketoester 11. Condensation of 11 with formamidine gives a 4-hydroxy pyrimidine 12, which can be converted into a 4-chloropyrimidine 13. Displacement of the chloride of 13 by an amine gives a desired 4-amino-pyrimidine 14.

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Scheme 4

An alternative synthesis of 4,6-disubstituted pyrimidines is illustrated in Scheme 5. In Scheme 5, nucleophilic substitution of an aryl fluoride 15 with an aryl thio under base-catalysis gives a biaryl sulfide 16. Transmetalation of 16 with $n-BuLi/ZnCl_2$, followed by Pd-catalyzed cross-coupling with a 4,6-diiodopyrimidine leads to an iodopyrimidine 17. Reaction of 17 with a selected amine gives a desired 4-aminopyrimidine 14.

Scheme 5

Yet another class of compounds of Formula I are compounds containing a pyridine ring, for example 2,4-disubstituted pyridines ($n=1$, $Y=C$, $B=N$, $Z=C$, $D=C$). Scheme 6 describes one procedure for the preparation of this class of compounds. In Scheme 6, Pd-catalyzed cross-coupling of a properly substituted 1-bromo-4-fluoro-benzene 15 and 4-pyridine boronic acid gives compound 18. Oxidation of 18 with MCPBA leads to a pyridinium oxide 19. Displacement of the fluoride of 19 with an aryl thio affords biarylsulfide 20. Treatment

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of **20** with POCl_3 , leads to 2-chloropyridine **21**. Finally, reaction of **21** with a selected amine gives a desired 2-aminopyridine **22**.

Scheme 6